

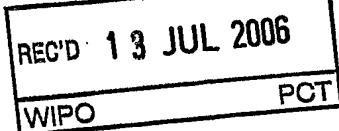
## PATENT COOPERATION TREATY


## PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference PB60808		<b>FOR FURTHER ACTION</b>		See Form PCT/PEA/416
International application No. PCT/US2005/010125		International filing date (day/month/year) 25.03.2005	Priority date (day/month/year) 25.03.2004	
International Patent Classification (IPC) or national classification and IPC INV. A61K31/00 A61K31/47 A61P25/18 A61P25/24				
Applicant SMITHKLINE BEECHAM CORPORATION et al.				
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input checked="" type="checkbox"/> sent to the applicant and to the International Bureau) a total of 1 sheets, as follows:</p> <p><input checked="" type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>				
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the report</p> <p><input checked="" type="checkbox"/> Box No. II Priority</p> <p><input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>				
Date of submission of the demand  12.10.2005		Date of completion of this report  12.07.2006		
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized officer  Pacreu Largo, M  Telephone No. +49 89 2399-7851		



**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/US2005/010125

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**Box No. I Basis of the report**

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1. With regard to the **language**, this report is based on
- ☒ the international application in the language in which it was filed
  - ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of:
    - ☐ international search (under Rules 12.3(a) and 23.1(b))
    - ☐ publication of the international application (under Rule 12.4(a))
    - ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))
2. With regard to the **elements\*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

**Description, Pages**

1-15 as originally filed

**Claims, Numbers**

1-4 as originally filed  
5 filed with telefax on 12.10.2005

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
  - ☐ the claims, Nos.
  - ☐ the drawings, sheets/figs
  - ☐ the sequence listing (*specify*):
  - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
  - ☐ the claims, Nos.
  - ☐ the drawings, sheets/figs
  - ☐ the sequence listing (*specify*):
  - ☐ any table(s) related to sequence listing (*specify*):

\* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
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**Box No. II Priority**

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1. ☐ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:
- ☐ copy of the earlier application whose priority has been claimed (Rule 66.7(a)).
  - ☐ translation of the earlier application whose priority has been claimed (Rule 66.7(b)).
2. ☒ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rule 64.1). Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

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**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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1. Statement

Novelty (N)	Yes: Claims	2-5
	No: Claims	1
Inventive step (IS)	Yes: Claims	
	No: Claims	1-5
Industrial applicability (IA)	Yes: Claims	1-5
	No: Claims	

2. Citations and explanations (Rule 70.7):

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
REPORT ON PATENTABILITY  
(SEPARATE SHEET)**

International application No.

PCT/US2005/010125

**Re Item II**

**Priority**

The priority n°60/553,391 is not considered to be rightfully claimed for the following reasons:

The priority document discloses the use of talnetant for the treatment of bipolar disorders. Present independent claims 1 and 5 refer to the use of an NK3 antagonist for the treatment of bipolar disorders.

Hence, at least part of the subject matter defined in the present claims is directed to a broader invention than that described in the cited priority document.

Document D6 (WO2005/014575) published after the claimed priority date but prior to the date of filing of the present application is therefore considered as part of the state of the art.

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. The documents cited in the International Search Report are consecutively numbered D1-D6 in the order of their listing. If not indicated otherwise, reference is made to the passages cited in said ISR.
2. The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 1 is not new in the sense of Article 33(2) PCT.

The document D1 discloses the use of the NK3 antagonist osanetant for the treatment of depressive disorders associated with bipolar disorders. According to document D6 (p.51, right-hand column), manic-depression was the former term used for bipolar disorders, and both bipolar I and II patients have a history of depression. Thus, it is more than doubtful that at least claim 1 is novel over D1.

Document D6 discloses the use of compounds structurally close to talnetant as NK3 antagonists. Some of the diseases mentioned to be treated by the compounds

includes bipolar manic depression, including type I and II, (p.10).

3. The subject-matter of claims 2 and 3 directed to the use of talnetant for the treatment of a bipolar disorder, as well as claims 4 and 5 directed to the treatment of specific manic episodes would appear to be novel, Art. 33(2) PCT.
4. In view of D1 and D6, it would be obvious for the skilled man willing to find alternative agents for the treatment of bipolar disorders to try to use other NK3 antagonists, such as talnetant, with a reasonable expectation of success.

Furthermore, the application does not contain any experimental evidence showing that talnetant is effective in the treatment of any specific bipolar disorder.

Even if an inventive step would be acknowledged for the use of talnetant in the treatment of bipolar disorders, the effect could not be generalized to any NK3 antagonist since there is no evidence for a link between the functionally defined compounds and the condition to be treated.

Therefore, the subject-matter of claims 1-5 does not involve an inventive step in the sense of Article 33(3) PCT.

5. The use of an NK3 antagonist in the manufacture of a medicament for the treatment or prevention of a disorder selected from the list:
- 296.00 Bipolar I Disorder, Single Manic Episode, Unspecified;
  - 296.01 Bipolar I Disorder, Single Manic Episode, Mild;
  - 296.02 Bipolar I Disorder, Single Manic Episode, Moderate;
  - 296.03 Bipolar I Disorder, Single Manic Episode, Severe without Psychotic Features;
  - 296.04 Bipolar I Disorder, Single Manic Episode, Severe with Psychotic Features;
  - 296.05 Bipolar I Disorder, Single Manic Episode, In Partial Remission;
  - 296.06 Bipolar I Disorder, Single Manic Episode, In Full Remission;
  - 296.40 Bipolar I Disorder, Most Recent Episode Hypomanic;
  - 296.40 Bipolar I Disorder, Most Recent Episode Manic, Unspecified;
  - 296.41 Bipolar I Disorder, Most Recent Episode Manic, Mild;
  - 296.42 Bipolar I Disorder, Most Recent Episode Manic, Moderate;
  - 296.43 Bipolar I Disorder, Most Recent Episode Manic, Severe without Psychotic Features;
  - 296.44 Bipolar I Disorder, Most Recent Episode Manic, Severe with Psychotic Features;
  - 296.45 Bipolar I Disorder, Most Recent Episode Manic, In Partial Remission;
  - 296.46 Bipolar I Disorder, Most Recent Episode Manic, In Full Remission;
  - 296.60 Bipolar I Disorder, Most Recent Episode Mixed, Unspecified;
  - 296.61 Bipolar I Disorder, Most Recent Episode Mixed, Mild;
  - 296.62 Bipolar I Disorder, Most Recent Episode Mixed, Moderate;
  - 296.63 Bipolar I Disorder, Most Recent Episode Mixed, Severe without Psychotic Features;
  - 296.64 Bipolar I Disorder, Most Recent Episode Mixed, Severe with Psychotic Features;
  - 296.65 Bipolar I Disorder, Most Recent Episode Mixed, In Partial Remission;
  - 296.66 Bipolar I Disorder, Most Recent Episode Mixed, In Full Remission;
  - 296.80 Bipolar Disorder NOS; and
  - 296.89 Bipolar II Disorder.